Influence of Cardiopulmonary Bypass on the State of Cognitive Functions in Patients with Ischemic Heart Disease

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Forty patients with ischemic heart disease and undergoing aortocoronary shunting surgery with cardiopulmonary bypass were studied. All patients were subjected to neuropsychological assessment and immunohistochemical analysis of the production of chemokines (IL-8, IP-10, MCP-1, MCP-3, MIP-1β, SDF-1α) and cytokines (TNF-α and IL-10). The aims of the study were to assess the presence and severity of cognitive deficit developing after surgery with cardiopulmonary bypass and to assess the effects of intraoperative Trasylol on its severity. Cognitive deficit on day 9 after coronary shunting with cardiopulmonary bypass was seen as impairments of attention, hearing-speech memory, visual memory, and dynamic praxis. Trasylol had a marked neuroprotective effect and suppressed the systemic inflammatory response. Patients given intraoperative Trasylol had no clinically significant cognitive deficit in the early post-operative period.

KEY WORDS: ischemic heart disease, cardiopulmonary bypass, cognitive functions.
Academy of Medical Sciences, from May 2000 to June 2002. Mean age was 52.6 ± 6.4 years and the mean duration of ischemic heart disease was 5.7 ± 0.4 years. The severity of stenocardia corresponded to grade III–IV. Study inclusion criteria were the absence of hemodynamically significant stenosis of the extracerebral vessels, profound focal brain lesions, mental, and acute neurological diseases, cardiac dysrhythmias, cardiac valve pathology, and cardiac aneurysms.

All patients underwent CS surgery with CPB. Anesthesia and perfusion were performed using standard methods developed in the Department of Anesthesiology and Cardiopulmonary Bypass Laboratory at the same center. Surgery was performed using hypothermia of 26°C. The duration of extracorporeal circulation was 115.9 ± 5.2 min. The duration of aortic clamping was 57.2 ± 3.3 min.

Patients were divided into two groups. The experimental group consisted of 20 patients given intraoperative Trasylol: an i.v. test dose of 10,000 KIU was given 10 min before the start of the main dose, which consisted of i.v. administration of 2·10⁶ KIU over 30–40 min between anesthesia and sternotomy, followed by a further 500,000 KIU one hour before the end of surgery. Furthermore, a dose of 2·10⁸ KIU was added to the volume of the primary loading of the CPB apparatus. The total dose was thus (5.5–7)·10⁶ KIU. A further 20 patients in whom surgery (CS) was performed in conditions of systemic hypothermia but without pharmacological treatment, made up the reference group. There were no significant differences between groups in terms of age, the duration and severity of ischemic heart disease, or the initial neurological neuropsychological status.

Neuropsychological assessment was performed before surgery and 7–9 days after surgery, as follows: 1) overall cognitive defect was assessed quantitatively using the Mini Mental State Examination (MMSE) scale; 2) complex (qualitative and quantitative) assessment of cognitive deficit was performed using the Frontal Assessment Battery (FAB); 3) The Schult test was used; 4) memory functions were assessed in terms of the immediate and delayed reproduction of auditory and visual material. These scales were used to calculate the cognitive deficit function Z using the principles described by Newman et al. [14] and Rasmussen et al. [15]; parameters such as attention, praxis, and memory were also assessed quantitatively.

Nine patients given Trasylol and nine patients from the reference group were selected for studies of the dynamics of chemokine production inducer tumor necrosis factor α (TNF-α) and the more powerful anti-inflammatory cytokin, known to suppress macrophage and dendritic cell function, interleukin-10 (IL-10).

Studies were performed using repeat serum samples collected from the internal carotid artery and jugular sinus for determination of jugulocarotid gradients of chemokine concentrations [13]. Chemokine levels were estimated in arterial and venous sera by immunoenzyne analysis (IEA) as specified by the manufacturer’s instructions (R&D Systems, Abingdon, UK). Serum IL-10 and TNF-α levels were estimated by IEA using antibodies from Becton Dickinson (Mountain View, USA). Integral assessments of the release of one or another chemokine during surgery was made from AUC (area under curve) values, this being the area beneath the plot describing chemokine release and the horizontal line representing the basal chemokine level in the individual patient.

Blood specimens were obtained at the following time points: 1) immediately after insertion of vascular catheters (basal level); 2) before CPB (before ischemia but after significant surgical trauma); 3) immediately before the end of CPB, i.e., before the end of the period of ischemia; 4) 3–5 min after the end of CPB (early reperfusion); and 5) 6 h after the end of CPB (late reperfusion). Results were analyzed statistically on a personal computer using the statistics program INSTAT.

RESULTS AND DISCUSSION

Aortocoronary shunting surgery led to improvements in the clinical state of all patients, with increases in exercise tolerance and myocardial systolic function. Complications occurred in two cases (one with a paroxysm of fibrillary arrhythmia developing on post-operative day 2 and one with pneumothorax). All patients were discharged in a satisfactory state at 10–15 days.

All patients showed disseminated neurological microsymptomatology in the early post-operative period, with oral automatism reflexes, central dysfunction of the facial and sublingual nerves, elements of dyscoordination and pyramidal syndromes, and oculomotor dysfunction.

Neuropsychological assessment showed that the incidence of clinically significant cognitive worsening in the early post-operative period was 30% in the reference group, compared with 38% in the Trasylol group. There were no statistically significant differences in the incidences of cognitive deficits between the groups (p > 0.05). The quantitative measure Z was 15.2 ± 2.8 in the reference group and 5.6 ± 2.1 in the patients given Trasylol. The difference between groups was statistically significant (p < 0.01).

The most frequent impairments demonstrated by patients during the post-operative period were reductions in memory, impairments to the dynamic organization of movement acts, and reduced attention. There were no significant differences in the structures of the cognitive defects between the two groups.